

WHAT IS CLAIMED IS:

1 1. An isolated nucleic acid encoding an ABCG8 polypeptide, said
2 polypeptide comprising an amino acid sequence that is at least about 70% identical to an
3 amino acid sequence as set forth in SEQ ID NO:4 or 8.

1 2. The nucleic acid of claim 1, wherein said polypeptide specifically
2 binds to polyclonal antibodies generated against a polypeptide that comprises an amino
3 acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:8.

1 3. The nucleic acid of claim 1, wherein said polypeptide comprises an
2 amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID
3 NO:8.

1 4. The nucleic acid of claim 1, wherein said polypeptide forms a
2 dimer with a second ABC polypeptide, and wherein said dimer exhibits sterol transport
3 activity.

1 5. The nucleic acid of claim 4, wherein said dimer is a heterodimer.

1 6. The nucleic acid of claim 4, wherein said sterol is cholesterol.

1 7. The nucleic acid of claim 5, wherein said second ABC polypeptide
2 is an ABCG5 polypeptide.

1 8. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 comprises an amino acid sequence that is at least about 70% identical to an amino acid
3 sequence as set forth in SEQ ID NO:2 or 6.

1 9. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 selectively binds to polyclonal antibodies generated against a polypeptide comprising an
3 amino acid sequence as set forth in SEQ ID NO:2 or 6.

1 10. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2
3 and SEQ ID NO:6.

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1 11. The nucleic acid of claim 7, wherein said ABCG5 polypeptide is
2 encoded by a nucleic acid that hybridizes under moderately stringent conditions to a
3 nucleic acid comprising a nucleotide sequence as set forth in SEQ ID NO:1 or 5.

1 12. The nucleic acid of claim 7, wherein said ABCG5 polypeptide is
2 encoded by a nucleic acid that comprises a nucleotide sequence that is at least about 70%
3 identical to a sequence as set forth in SEQ ID NO:1 or 5.

1 13. The nucleic acid of claim 1, wherein said nucleic acid hybridizes
2 under moderately stringent hybridization conditions to a nucleic acid comprising a
3 nucleotide sequence as set forth in SEQ ID NO:3 or 7.

1 14. The nucleic acid of claim 13, wherein said nucleic acid hybridizes
2 under stringent hybridization conditions to a nucleic acid comprising a nucleotide
3 sequence as set forth in SEQ ID NO:3 or 7.

1 15. The nucleic acid of claim 1, wherein said nucleic acid comprises a
2 nucleotide sequence at least about 70% identical to a sequence as set forth in SEQ ID
3 NO:3 or 7.

1 16. The nucleic acid of claim 1, wherein said nucleic acid comprises a
2 nucleotide sequence as set forth in SEQ ID NO:3 or 7.

1 17. The nucleic acid of claim 1, wherein said nucleic acid is from a
2 mouse or a human.

1 18. The nucleic acid of claim 1, wherein said nucleic acid is expressed
2 in the intestine or in the liver in the presence of an LXR agonist.

1 19. The nucleic acid of claim 1, wherein said nucleic acid is expressed
2 in a tissue selected from the group consisting of liver, jejunum, ileum, and duodenum.

1 20. An expression cassette comprising the nucleic acid of claim 1
2 operably linked to a promoter.

1 21. An isolated cell comprising the expression cassette of claim 20.

1 22. An isolated ABCG8 polypeptide, said polypeptide comprising an
2 amino acid sequence that is at least about 70% identical to an amino acid sequence as set
3 forth in SEQ ID NO:4 or 8.

1 23. The isolated polypeptide of claim 22, wherein said polypeptide
2 selectively binds to polyclonal antibodies generated against a polypeptide comprising an
3 amino acid sequence as set forth in SEQ ID NO:4 or 8.

1 24. The isolated polypeptide of claim 22, wherein said polypeptide
2 comprises an amino acid sequence as set forth in SEQ ID NO:4 or 8.

1 25. The isolated polypeptide of claim 22, wherein said polypeptide
2 forms a dimer with a second ABC polypeptide, and wherein said dimer exhibits sterol
3 transport activity.

1 26. The isolated polypeptide of claim 25, wherein said dimer is a
2 heterodimer.

1 27. The isolated polypeptide of claim 26, wherein said second ABC
2 polypeptide is ABCG5.

1 28. The isolated polypeptide of claim 27, wherein said ABCG5
2 polypeptide comprises an amino acid sequence that is at least about 70% identical to an
3 amino acid sequence as set forth in SEQ ID NO:2 or 6.

1 29. The isolated polypeptide of claim 27, wherein said ABCG5
2 polypeptide selectively binds to polyclonal antibodies generated against a polypeptide
3 comprising an amino acid sequence as set forth in SEQ ID NO:2 or 6.

1 30. The isolated polypeptide of claim 27, wherein said ABCG5
2 polypeptide comprises an amino acid sequence selected from the group consisting of
3 SEQ ID NO:2 and SEQ ID NO:6

1 31. The isolated polypeptide of claim 25, wherein said sterol is
2 cholesterol.

1 32. The isolated polypeptide of claim 22, wherein said polypeptide is
2 expressed in the intestine or in the liver in the presence of an LXR agonist.

1 33. The isolated polypeptide of claim 22, wherein said polypeptide is
2 expressed in a tissue selected from the group consisting of the liver, jejunum, ileum, and
3 duodenum.

1 34. The isolated polypeptide of claim 22, wherein said polypeptide is
2 from a mouse or a human.

1 35. An antibody generated against the isolated polypeptide of claim 22.

1 36. A method of making an ABCG8 polypeptide, the method
2 comprising:
3 (i) introducing a nucleic acid of claim 1 into a host cell or cellular extract;
4 and
5 (ii) incubating said host cell or cellular extract under conditions such that
6 said ABCG8 polypeptide is expressed in the host cell or cellular extract.

1 37. The method of claim 36, further comprising recovering the ABCG8
2 polypeptide from the host cell or cellular extract.

1 38. A method of identifying a compound useful in the treatment or
2 prevention of a sterol-related disorder, said method comprising contacting an ABCG8
3 polypeptide with a test agent, and determining the functional effect of said test agent upon
4 said polypeptide, wherein a functional effect exerted on said polypeptide by said test
5 agent indicates that said test agent is a compound useful in the treatment or prevention of
6 said sterol-related disorder.

1 39. The method of claim 38, wherein said sterol is cholesterol.

1 40. The method of claim 38, wherein said polypeptide comprises an
2 amino acid sequence that is at least about 70% identical to an amino acid sequence as set
3 forth in SEQ ID NO:4 or 8.

1 41. The method of claim 38, wherein said polypeptide is present in a
2 cell or cell membrane.

1 42. The method of claim 38, wherein said polypeptide is bound to a
2 heterologous ABC polypeptide, forming a heterodimer.

1 43. The method of claim 38, wherein said functional effect comprises
2 an increase in the sterol transport activity of said polypeptide.

1 44. The method of claim 38, wherein said functional effect comprises a
2 physical interaction between said test agent and said polypeptide.

1 45. The method of claim 44, wherein said physical interaction is
2 detected using a direct binding assay.

1 46. The method of claim 38, wherein said sterol-related disorder is
2 sitosterolemia.

1 47. The method of claim 38, wherein said sterol-related disorder is
2 selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones,
3 HDL deficiency, atherosclerosis, and nutritional deficiencies.

1 48. A method of identifying a compound useful in the treatment or
2 prevention of a sterol-related disorder, said method comprising contacting a cell that
3 expresses or is capable of expressing an ABCG8 polypeptide with a test agent, and
4 determining the functional effect of said test agent upon said cell;
5 wherein a functional effect exerted on said cell by said test agent indicates
6 that said test agent is a compound useful in the treatment or prevention of said sterol-
7 related disorder.

1 49. The method of claim 48, wherein said sterol is cholesterol.

1 50. The method of claim 48, wherein said ABCG8 polypeptide
2 comprises an amino acid sequence that is at least about 70% identical to an amino acid
3 sequence as set forth in SEQ ID NO:4 or 8.

1 51. The method of claim 48, wherein said compound produces an
2 increase in the expression of an ABCG8 gene that encodes said ABCG8 polypeptide.

1 52. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 mRNA in said cell.

1 53. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 polypeptide in said cell.

1 54. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 protein activity in said
3 cell.

1 55. The method of claim 48, wherein said compound modulates the
2 level of sterol transport activity in said cell.

1 56. The method of claim 55, wherein said sterol transport activity in
2 said cell is detected by detecting the rate of sterol efflux in said cell.

1 57. The method of claim 56, wherein said sterol is cholesterol.

1 58. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is mediated by LXR or RXR.

1 59. The method of claim 48, wherein said sterol-related disorder is
2 sitosterolemia.

1 60. The method of claim 48, wherein said sterol-related disorder is
2 selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones,
3 HDL deficiency, atherosclerosis, and nutritional deficiencies.

1 61. A method of treating or preventing a sterol-related disorder in a
2 mammal, said method comprising administering to said mammal a compound that
3 increases the level of expression or activity of an ABCG8 polypeptide in a plurality of
4 cells of said mammal.

1 62. The method of claim 61, wherein said sterol is cholesterol.

1 63. The method of claim 61, wherein said sterol-related disorder is
2 sitosterolemia.

1 64. The method of claim 61, wherein said sterol-related disorder is
2 selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones,
3 HDL deficiency, atherosclerosis, and nutritional deficiencies.

1 65. The method of claim 61, wherein said compound produces a
2 decrease in the amount of dietary sterol that is absorbed in said mammal.

1 66. The method of claim 61, wherein said compound produces a
2 decrease in the amount of sterol that is retained in the liver of said mammal.

1 67. The method of claim 61, wherein said compound is identified using
2 the method of claim 38 or 48.

1 68. The method of claim 61, wherein said compound causes an
2 increase in LXR or RXR activity within cells of said mammal.

1 69. A method of prescreening to identify a candidate therapeutic agent
2 that modulates ABCG8 activity in a mammal, the method comprising:
3 providing a cell which comprises an ABCG8 polypeptide; and
4 a test compound; and
5 determining whether the amount of sterol transport activity in said cell is
6 increased or decreased in the presence of the test compound relative to the activity in the
7 absence of the test compound;

8 wherein a test compound that causes an increase or decrease in the amount
9 of sterol transport activity is a candidate therapeutic agent for modulation of ABCG8
10 activity in a mammal.

1 70. The method of claim 69, further comprising a secondary step, wherein
2 said test compound is administered to a mammal, and the absorption of dietary sterol in said
3 mammal is detected.